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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/691,405	10/17/2000	Steven R. Binder	2558B-063700US	3942

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EXAMINER	
ALLEN, MARIANNE P	
ART UNIT	**PAPER NUMBER**
1631	10

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/691,405	BINDER ET AL.	
	Examiner	Art Unit	
	Marianne P. Allen	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-10 and 12-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1-2, 5-10, 12-18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/1/03 has been entered.

Claims 17-18 have been newly added. Claims 1-2, 5-10, 12-18 are under consideration.

Claim Rejections - 35 USC § 112

Claims 1-2, 5-10, and 12-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has substantively amended claims 1-2 and introduced new claims 17-18. No basis has been pointed to for these amendments and new claims and none is apparent. Note that the original claims required identification of the particular autoimmune disease(s) and the present claims require determining whether the test subject is suffering from one or more autoimmune diseases but not determining which one(s). The specification does not appear to disclose the concept of a "k-nearest neighbor process." It is unclear if this phrase is limited to a particular algorithm such as that generally described on page 5 and the metes and bounds do not appear to be set forth in the specification. In addition, claims 1 and 17, although using slightly different

wording, appear to be directed to identical methods. Applicant is requested to distinguish between these two claims.

Should this new matter rejection be overcome, the following enablement rejection would still apply to the claims.

The claims are directed to a method of identifying whether a test subject is suffering from one or more systemic autoimmune diseases by receiving a test data set for the test subject, storing a plurality of reference data sets for reference subjects, and comparing the test data set and reference data set by applying a k-nearest neighbor process to produce a statistically derived decision indicating whether the test subject is suffering from one or more autoimmune diseases. Dependent claim 2 requires a statistically derived decision indicating whether the test subject is suffering from two autoimmune diseases. New claim 17 is directed to a method of diagnosis with essentially the same steps as claim 1.

The specification details the difficulties in diagnosing autoimmune disorders based upon transient symptoms, overlapping symptoms, variations in normal antibody levels, and so forth.

The specification lists a variety of autoimmune diseases and lists a variety of antigens (see pages 7-8). However, the specification does not associate any antigen (or autoantibody) with any particular disease with respect to presence (or absence) and/or amounts. Nor does the specification disclose how discrimination between different autoimmune diseases, particularly with those that involve overlapping autoantibodies, is to be implemented. Applicant's reliance upon Peter et al. (referenced on page 7 of the specification) remains an improper incorporation by reference of essential material. It is noted that applicant's arguments indicate that they are unaware of how many autoantibodies are disclosed by Peter et al. They have provided no

reasoning in support of the assertion that it would be routine to identify additional autoantibodies that could be used in developing the claimed method. The specification provides no guidance as to determining unknown autoantibodies related to the named systemic autoimmune diseases. It is further noted that Peter et al. is not of record and so what it teaches or does not teach with respect to the claimed methods cannot be evaluated by the examiner.

The recitation of "k-nearest neighbor process" does not provide guidance to one of ordinary skill in the art to developing the claimed computer-implemented method. Again, this recitation does not represent, for example, a complete commercially available algorithm, program or system where applicant must merely supply a specified type of data for analysis. This is not a situation where new data is input into known programs for solving the problem. That is, applicant is not using known software to solve a known problem in a conventional manner where one practicing the invention need only supply the data to be analyzed. Known statistical techniques will need to be adapted to solve this particular problem. However, the specification has not exemplified any method for identification within the claims nor provided guidance on the how to adapt the known statistical techniques for solving the problem of identifying systemic autoimmune disease in a subject. One of ordinary skill in the art would be required to make independent decisions and judgments on how to apply the statistical techniques, what parameters to use or change, assumptions to make, and so forth. Any model developed must be tested and validated. This is not considered to be routine experimentation. This is an invitation to experiment and to develop applicant's claimed method. The specification provides no training set with the information required to produce statistically derived decisions with respect to systemic autoimmune diseases. The reference data must be collected and evaluated,

assumptions as to what specific data will be used must be made (including what specific attributes to analyze, how they will be analyzed, which algorithms to use), and the composition of the training set and test sets and so forth must be determined. The specification does not exemplify any implementation of the claimed methods and provides no specific guidance for doing so.

In contrast, Cabello et al. discloses k-nearest neighbor analysis with respect to ventricular arrhythmia detection. Cabello et al. discloses using a set of 90 ECG signal segments with specifically defined spectral parameters in the analysis and the test and learning sets are described (see at least page 78, second full paragraph, and page 83). The instant specification provides no such test sets, learning sets, or parameters.

In contrast, Tobin et al. discloses a feature-based, fuzzy k-nearest neighbor classifier and optimization techniques. The classifiers and training data are disclosed. In each case, the datasets are well characterized. (See at least section 2 and 3.1.) The instant specification does not provide this type of information and how to apply it to diagnosis of systemic autoimmune diseases.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In the instant application, a great deal of experimentation would be required that is not routine. The specification provides no direction or guidance on how to adapt a "k-nearest neighbor process" to solve their particular problem. There are no working examples. Computational methods of diagnosis are quite complicated such that even though the skill of those in the art is high, such inventions are difficult to develop and validate. Note that none of the prior art identified by applicant concerns diagnosis of any disease using any antibody profiles and a k-nearest neighbor process. Again, the specification does not associate any antigen (or autoantibody) with any particular disease with respect to presence (or absence) and amounts. That is, the specification does not exemplify any embodiment of the claimed method. Nor does the specification disclose how discrimination between different autoimmune diseases, particularly with those that involve overlapping autoantibodies, is to be implemented. (See Thompson et al., 1993, which documents the difficulties in distinguishing autoantibody profiles in systemic autoimmune diseases.) Finally, the breadth of the claims remains broad for many aspects of the claims from the particular k-nearest neighbor process, to the number and type of autoantibodies in the test data and library of reference data sets, to the diseases to be identified.

Applicant is invited to point to the portion of the specification that associates the particular autoantibodies and particular levels of those autoantibodies that define each of the systemic autoimmune diseases recited in the claims, particularly with respect to the antibodies required by claims 5-8. Applicant is invited to point to the portion of the specification that provides the appropriate reference data set(s) required by the claims, particularly with respect to the biological samples required by claims 9-10.

In conclusion, it would constitute undue experimentation to practice the method as claimed and applicant's specification is an invitation to experiment to develop the claimed method.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is inconsistent and confusing in reciting "said one or more systemic autoimmune diseases consists of systemic lupus erythmatosus." A single disease cannot be more than one.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa